Maternal and infant outcomes after different methods of umbilical cord management

Article (Published Version)

EDITORIAL

Maternal and Infant Outcomes After Different Methods of Umbilical Cord Management

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Clamping and cutting the umbilical cord immediately after birth of an infant was introduced as an intervention in the mid-20th century concurrent with a change from home to hospital deliveries, without consideration of maternal or fetal effects.[1] In the late 1960s, several studies explored the physiology of the placenta-fetal transfusion, examining the effects of the time between delivery of the infant and cord clamping and cutting, of lowering the infant below the placental level to make use of gravity, and of uterotonics (such as oxytocin) and uterine contractions.[2-4] In the 1980s, the Bristol third-stage trial involving 1695 women included early cord clamping as one part of active management of the third stage of labor for reducing postpartum hemorrhage but without evidence that cord clamping was a necessary component for active management.[5] More recently, randomized clinical trials have demonstrated benefits of cord management by delayed cord clamping or umbilical cord milking for both preterm and term infants.[6] A Cochrane review of studies involving preterm infants found a 28% reduction in in-hospital deaths associated with delayed cord clamping.[6] Among term infants, higher iron values during the first year of life and better neurodevelopmental outcomes up to 4 years, especially in boys, have been reported.[7,8] The evidence led the World Health Organization to publish recommendations to delay cord clamping and cutting for at least 60 seconds for preterm infants and 1 to 3 minutes for term infants to allow for placental transfusion to take place.[9] Two studies in *JAMA* provide new data on the effects of umbilical cord interventions on women undergoing cesarean delivery at term and the effects on preterm infants.

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Most studies that have evaluated the maternal effects of umbilical cord interventions have been based on vaginal deliveries, and the efficacy of placental blood transfer to infants delivered by cesarean remains controversial. The catecholamine levels in newborns delivered by cesarean are low, in contrast to the surge of catecholamines that occurs in infants delivered vaginally, resulting in impaired lung adaption and a higher rate of hypoglycemia.[10] In addition, maternal uterine contractions do not begin as rapidly following cesarean vs vaginal delivery, raising clinical concern about postpartum hemorrhage in these women.[11]

The study by Purisch and colleagues[12] addresses these concerns through a well-conducted randomized clinical trial comparing immediate cord clamping with a delay of 60 seconds in 113 women undergoing elective cesarean delivery at term. The study was powered to detect a significant difference between groups in maternal blood loss by comparing antenatal and postnatal hemoglobin values. The preoperative maternal hemoglobin level was 12.0 g/dL in the delayed group and 11.6 g/dL in the immediate group; the postoperative hemoglobin level was 10.1 g/dL in the delayed group vs 9.8 g/dL in the immediate group, with no significant difference in the change in hemoglobin level between groups (mean difference, 0.12 g/dL [95% CI, −0.22 to 0.46]; $P = .49$). No significant adverse events were seen in the women.

Although the safety of placental transfusion for the mother seems well established, it remains unclear which method of providing placental transfusion is best for the infant: delayed clamping and cutting the cord or milking the intact cord. The latter provides a transfusion more rapidly, which may facilitate initiation of resuscitation when needed.

The study by Katheria and colleagues[13] aimed to address the question of whether umbilical cord milking was noninferior to delayed cord clamping in providing placental transfusion to very preterm infants less than 32 weeks' gestation. The study was terminated early when an interim statistical analysis showed an excess of infants with severe intraventricular hemorrhage in the umbilical cord milking group (8% vs 3% with delayed cord clamping; risk difference, 5% [95% CI, 1%-9%]; $P = .02$). The mortality rate was not statistically significantly different between groups (7% with umbilical cord milking vs 6% with delayed cord clamping). The increase in severe intraventricular hemorrhage occurred in the subgroup of preterm infants 23 to 27 weeks' gestational age (22% with umbilical cord milking vs 6% with delayed cord clamping; risk difference, 16% [95% CI, 6%-26%]; $P = .002$) but not in infants of older gestational age.

The mortality rates are similar to those reported in the Cochrane review.[6] The incidence of severe intraventricular hemorrhage of 8% in the umbilical milking group is higher than the 5.2% (6 studies, n = 307) reported in the Cochrane review, while the 3% incidence for the delayed clamping group is lower than the 4.5% (9 studies, n = 992) observed in the Cochrane review. In addition, a recent trial by Shirk et al[14] that included 204 preterm infants between 23 and 34 weeks' gestation found no statistically significant differences in neonatal outcomes (hematocrit, intraventricular hemorrhage, necrotizing enterocolitis, transfusions, and death) between the 2 methods of placental transfusion. In particular, there were no statistically significant differences in the incidence of intraventricular hemorrhage in the subgroup of infants born at 23 to 27 weeks' gestation.

Clinicians and researchers are discussing whether umbilical cord milking, through which blood is literally pushed into

the fragile circulatory system of a premature infant, can be regarded as a physiological means of transitioning to extrauterine life. In an experimental study, Blank et al[15] showed that umbilical cord milking with intermittent cord occlusion caused large fluctuations in mean carotid artery pressure and blood flow in prematurely delivered lambs. While some authors have suggested an association between a sudden increase in circulating blood volume with umbilical cord milking as a cause of intraventricular hemorrhage, others have proposed that insulinlike growth factor-1[16] or antenatal factors, such as chorioamnionitis, may play a role in the pathophysiology. Umbilical cord milking has been used in many hospitals without an increase in intraventricular hemorrhage being observed. In addition, the trials by Shirk et al[14] and Katheria et al[13] had different results, and the trial by Katheria et al had various limitations (eg, early termination and post hoc analysis). Therefore, further studies of umbilical cord milking should only be conducted once the results of the ongoing trials are reported, especially for infants at 23 to 27 weeks' gestational age. The signal of harm detected in the trial by Katheria et al suggests delayed cord clamping should be considered over umbilical cord milking for these smallest infants unless quick resuscitation is anticipated, and then careful monitoring of important outcome measures would be required. Investigations of umbilical cord milking and delayed cord clamping for infants of older gestational age, including follow-up of those from the trial of Katheria et al, are needed.

The study by Purisch et al demonstrated the safety of delayed cord clamping for mothers delivering by cesarean at term. However, the safest method for enhancing placental transfusion in preterm infants remains unclear not only in terms of delayed cord clamping vs umbilical cord milking, but also in the duration of delay, the positioning of the infant with regard to the placenta, the number of times the intact cord should be milked, and the use of uterotonics. A standardization of the techniques should be defined and can then be studied and refined to develop guidance about the optimal bundle of interventions. An international effort is under way to use individual patient data analysis to compare reported methods of placental transfusion with immediate cord clamping to identify the best techniques (ACTRN12619001305112). In the meantime, clinicians should follow the World Health Organization recommendation to delay cord clamping and cutting for 1 to 3 minutes for term infants and for at least 60 seconds for preterm infants to prevent iron deficiency and potentially enable more premature infants to survive.

ARTICLE INFORMATION

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Conflict of Interest Disclosures: None reported.

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